



Case Report

Evaluation of a fatal propofol intoxication due to self administration

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ARTICLE INFO

Article history:

Received 24 July 2008

Received in revised form 20 October 2008

Accepted 11 December 2008

Available online 23 January 2009

Keywords:

Forensic science

Propofol intoxication

Toxicological evaluation

Gas chromatography–mass spectrometry

ABSTRACT

Propofol is a short acting intravenous anaesthetic, active agent of Diprivan. The abuse potential of propofol has not completely defined, but there are anecdotal case reports in the literature about propofol abuse and dependency. This report presents a fatal case of a middle age female victim who died of self-administered propofol intoxication. The propofol level of the blood sample was measured with gas chromatography–mass spectrometry after liquid–liquid extraction. The results of toxicological investigation suggested that death was not directly caused by propofol intoxication, however, based on the pathomorphological changes detected during the medico-legal autopsy we supposed that the fatal outcome was resulted by respiratory depression after rapid injection.

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1. Introduction

Propofol (2,6-diisopropylphenol) is a short acting intravenous anaesthetic, active agent of Diprivan (Astra Zeneca). The drug, an alkylphenol, formulated in an oil-in-water emulsion is chemically distinct from currently available, i.v., anesthetic agents. It has high lipophilic property with a fast onset and short duration of the narcotic effect. The following drug forms are available in Hungary: infusion (1% and 2%, 50 ml) and injection (1%, 20 ml). The pharmacokinetics of propofol are well described by a three compartment linear model with compartments representing the plasma, rapidly equilibrating tissues, and slowly equilibrating tissues.

Following an, i.v., bolus dose, there is rapid equilibration between the plasma and the highly perfused tissue of the brain, thus accounting for the rapid onset of anesthesia. Due to repeated injection after every arousal, propofol accumulation in brain cannot be observed because of its fast redistribution. Propofol is majority metabolized by conjugation in the liver to inactive metabolites which are excreted by the kidney. Propofol-glucuronide accounts for about 50% of the administered dose. The remainder consists of the 1- and 4-glucuronide and 4-sulfate conjugates of 2,6-diisopropyl-1,4-quinol.¹

We present a fatal case of a middle age female victim who died of respiratory depression caused by self-administered propofol intoxication.

2. Case report

2.1. Anamnestic data

A 42-year-old anaesthetic nurse was found without vital signs at her home, in her bed lying on the back in a state of nature. Scene investigation was performed by the police. Next to the body 14 empty ampoules of Diprivan (200 mg/20 ml propofol per ampoule) and two full syringes (20 ml) with Diprivan were found. Anamnestic data collected from the family members suggested that the victim used propofol every day for the purpose of narcotic. Suicide notes were not found. She had not any previous suicide attempts. There was not psychiatric treatment in the anamnestic data.

2.2. Autopsy results

During the autopsy knot of thyroid gland, and signs of skives on the joints were found. There was a cannula with 20 ml syringe in small vessel of the right thigh (Fig. 1). More than a half part of syringe was filled by Diprivan. A haemorrhage around the small vessel in the fat tissue, pulmonary oedema, and brain oedema, moderate fatty liver and some plaques on coronary arteries were detected. During the autopsy we reserved biological sample from the peripheral blood (from femoral vein) for toxicological investigation. There was no urine in the bladder.

2.3. Toxicological findings

Toxicological investigations were performed in the Toxicological Laboratory of our department. To prevent loss of propofol we analyzed the blood sample without delivery.

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Fig. 1. 42-Year-old female anaesthetic nurse was found dead at home. A cannula with 20 ml syringe was observed in the small vessel of the right thigh.

2.3.1. Sample pretreatment

1 ml of postmortem blood sample was pipetted into a 10 ml glass tube, 50 μ l of thymol solution (internal standard, Ph. Eur. quality, 10 μ g/ml in methanol), 1 ml of acetone, and 0.2 M zinc-sulfate solution were added and mixed. After centrifugation, the supernatant was pipetted into a glass tube and 1 ml of borate buffer (pH 9) was added, and mixed. Then 3 ml of chloroform–ethyl acetate (70:30) mix was added and extracted for 3 min. on a vortex mixer.² After centrifugation (2500 rpm, 10 min) the organic layer was evaporated to dryness under a gentle stream of nitrogen. The residue was reconstituted with 100 μ l of ethyl acetate and 1 μ l aliquot was injected to the chromatographic system in splitless mode.

2.4. Chromatographic conditions

To measure the propofol level of blood sample, an Agilent 6890 gas chromatograph coupled with Agilent 5973 quadrupole mass spectrometer was used in electron impact mode. The separation was achieved on a Supelco SPB-624 fused silica capillary column (30 m \times 0.25 mm) with 1.4 μ m film thickness. The column temperature was maintained at 55 $^{\circ}$ C and increase to 220 $^{\circ}$ C at 10 $^{\circ}$ C/min. The injection port and the transfer line temperature was 240 and 220 $^{\circ}$ C respectively. Helium (6.0) was used as carrier gas with flow rate of 1 ml/min. The qualitative analysis was performed in scan mode with the mass range of 70–200 amu. For quantitation the MS was operated in SIM mode with the following ion settings: Thymol: m/z 135, 150 and 91; Propofol: m/z 163, 178 and 117. The cal-

ibration range was 50–1500 ng/ml, coefficient of determination of the calibration curve was 0.993.

3. Discussion

We present a fatal case of an accidental propofol overdose of an anaesthetic nurse. The toxicological examination revealed the presence of propofol (92% mass spectra correspondence to the NIST library) in concentration of 1.31 μ g/ml. Propofol was also detected in the needle and cannula. BAC test resulted very light alcohol influence (0.78 g/l). Other pharmacologically relevant substances were not detected in blood sample.

To assess the relevance we compared our results on propofol concentrations with other four fatal cases reported in the literature.^{3–6} In these four cases the victims were also health care professionals. Table 1 demonstrates the postmortem blood concentrations of propofol detected at therapeutic level in all cases.

The standard dose of propofol is 2–2.5 mg/kg body weight for the induction of anaesthesia within 1–2 min and arousal after 5–10 min.⁵ After a bolus injection, patients lose consciousness at blood concentrations of 1.3–6.8 μ g/ml and regain it through fast redistribution at concentrations of 1–2.5 μ g/ml. The onset of unconsciousness and CNS depression are also known to be related to the speed of injection.⁴ The mechanism of action is not completely known, however, the drug probably exerts its pharmacological effects by enhancing the function of the GABA-activated chloride channel.⁷ In CNS propofol has euphoric feelings, sexual hallucinations and has sedative and relaxing effects.^{8–11} Its euphoric effects are clinically known and have also been demonstrated in a double blind randomized study in healthy volunteers using propofol in subanaesthetic dosages (0.2–0.6 mg/kg). The authors of this study concluded that use of propofol may be rewarding in some people without history of drug abuse.¹²

Soyka and Schütz¹³ also described a case study of a 31-year-old general practitioner, who injected propofol himself on daily base during 10 months. They reported rapidly experienced mild euphoria and feeling of relaxation during initial injections, followed by strong sedation and loss of consciousness. The victim had retrograde amnesia especially for the repeated injection procedure, which was more than 100 times/day because the drug effect lasted not more than 5–10 min. There was almost complete lack of withdrawal signs and an intensive craving made it impossible to stop using the substance.

Propofol administration in subanaesthetic doses was novel, it was used increasingly to treat migraine and other headaches.¹⁴ Fritz¹⁵ described a case of propofol dependency in a lay person, who had tension headache, which was treated with propofol by an anaesthesiologist. He started to inject himself with 3–4 occasions per week, lasting 1–2 h. After he accidentally injected an overdose of this drug, he was found unconscious and cyanotic.

Hypotension, airway obstruction, oxygen desaturation, especially with a rapid bolus injection may be detected as cardiorespiratory side effects of propofol intoxication. Apnoea can be more frequently observed during the induction of anaesthesia with pro-

Table 1
Propofol concentrations in blood reported in the literature and in our case.

	Reported cases	Blood concentration (μ g/ml)
Drummer ⁴	29-Year-old female radiographer	0.22
Chao ³	37-Year-old male medical doctor	2.5
Iwersen-Bergmann ⁵	26-Year-old male nurse	5.3
Kranioti ⁶	38-Year-old female anaesthesiologist	2.4
Our case	42-Year-old female anaesthetic nurse	1.31

propofol compared with other anaesthetics and its duration is usually short, but it can persist for up to 3 min.¹

Kranioti et al.⁶ described a case when the victim was also an anesthesiologist. With our case it suggests that accidental intoxication due to propofol abusing is a very rare event because this drug is distributed mostly amongst medical personnel so the professionals working with this drug have a special risk for accidental overdose. The health professionals suffered accidental intoxication based on some information about the pharmacology but not deep knowledge enough.

After the evaluation of the results of the scene investigation, the pathomorphological changes and the toxicological results the question has been raised: was this case an accidental or a suicidal death? In our case the anamnestic data suggested that the victim had not any previous suicide attempts and she was not under psychiatric treatment. Information collected from family members supposed that the victim used propofol every day for the purpose of narcotic. To support this assertion, during the scene investigation 14 empty ampoules of Diprivan were found next to the body. None of the presented cases of propofol intoxications have found evidences for suicidal attempt.^{3–6} We confirmed study results that the propofol intoxication is a very rare event and cause accidental fatal complications. Due to the rapid onset, it is not clear whereby can the victim self-administer the deadly dose before losing consciousness. Possibly it has been administered by a third party. Based on all the information we concluded our victim had suffered accidental death by respiratory depression after rapid injection.

4. Conclusions

Evaluation of the pharmacological effects and the pathophysiology during propofol intoxication represents a challenge for the toxicologists and forensic pathologists. We have to emphasize the importance of toxicological examination in every sudden unexpected death of people during the process of medico-legal investigation. The abuse potential and forensic importance of propofol have not completely been established, just a few publications have been reported about propofol abuse and dependency. According to the literature, anaesthesiologists have higher incidence of propofol abusing because this drug has been widely used in clinical practice. Due to the short duration of action, the abuse of this drug is very easy to suppress.

Conflict of interest statement

All authors have made a significant contribution to the findings and methods in the paper. There are no financial or commercial interest. The work has not been published and has not been submitted simultaneously to any other journal.

Funding

None declared.

Ethical approval

None declared.

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